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10/587,831	07/28/2006	**Frank Vitzthum**	05552.1470	6928

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EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,831	VITZTHUM, FRANK	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,16 and 17* is/are pending in the application.

4a) Of the above claim(s) *13 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/24/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions and Amendments to the Claims

1. This action is in response to papers filed 24 March 2009 in which claims 1-13 and 16-17 were amended, claims 14-15 were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

2. Applicant's election of Group I in the reply filed on 2 March 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 13 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2 March 2009.

4. Claims 1-12 and 17 are under prosecution.

Foreign Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The Information Disclosure Statement filed 24 March 2009 is acknowledged. However, only the Abstract of Document DE 10007531 A1 is being considered because an English language translation of the remainder of the document has not been provided. The document of Hintsche is not being considered because it is not in English.

Specification and Drawings

7. The amendment filed 28 July 2006 (hereafter "Applicant's Amendments") is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

A. Applicant's amendments to page 1 of the specification state that PCT/EP/2005/000906 and DE 10 2004 004 882.7 are "incorporated herein by reference." The English language National Stage specification as originally filed does not state that the applications are incorporated by reference. In addition, the PCT of this National Stage Application (WO 2005/073403 A1) does not state that DE 10 2004 004 882.7 is incorporated by reference. Thus, the statement that the applications are incorporated by reference constitutes new matter.

In addition, it is noted that 37 CFR 1.57(c) and (d) explicitly state that only nonessential material may be incorporated by reference to a foreign patent or foreign published application.

B. Applicant's amendments to page 63 of the specification have changed to 5th exemplary embodiment from "G6PDH x thrombin" to a DNA aptamer. Thrombin is a coagulation protein, not a DNA sequence. In addition, page 51 of WO 2005/073403 A1 also refers to "G6PDH x Thrombin," and not to a DNA aptamer. Therefore, the amendment changing the thrombin protein to a DNA aptamer sequence constitutes new matter.

C. Applicant's amendments to page 68 of the specification state that it is possible for selective components to be combined with the exemplary embodiments described in "the present specification." However, the English language National Stage specification as originally filed states that the exemplary embodiments described in "MA 1250." Thus, English language National Stage specification as originally filed does not contain a statement regarding combinations based on "the present specification." In addition, page 54 of WO 2005/073403 A1 also refers to "MA 1250." Further, neither specification as originally filed equates "MA 1250" with the instant specification or even describe what "MA 1250" is. Therefore , the recitation of the possibility of selective components to be combined with the exemplary embodiments described in "the present specification" constitutes new matter.

D. New Figures 15 and 16 are also objected to under 35 U.S.C. 132(a) because they introduce new matter into the disclosure. While pages 43-44 of the National Stage entry of the specification as originally filed contain a generic description of Figures 15 and 16, and while page 36 of the PCT Application Publication No. WO 2005/073403 A1 refers generically to "Abbilidungen 15 und 16," the PCT Application as originally filed does not contain Figures (i.e., "Abbilidungen") 15 or 16. Therefore, the specific embodiments depicted in Figures 15 and 16 were not present in the PCT as originally filed, and each of Figures 15 and 16 therefore constitute new matter.

E. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Interpretation

8. Claims 1-12 are drawn to a "system." As noted in the previous Requirement for Restriction mailed 25 February 2009, the specification teaches a "system" wherein the "system" is defined in terms of **structural** limitations (e.g., page 4). In addition, claims 1-12 recite **structural** limitations of the "system." Thus, the "system" is interpreted to encompass any collection of reagents and parts used together that are not necessarily part of a completely integrated single unitary device. Any further interpretation of the word is considered an "intended use" and does not impart any further structural limitation on the claimed subject matter.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-10, 12, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Miller et al (U.S. Patent Application Publication No. US 2004/0018492 A1, published 29 January 2004).

Regarding claim 1, Miller et al teach an analytical test system comprising a switch probe in the form of the probe of Figure 6, which comprises a probe in the form of a DNA portion and a catalytic component in the form of an enzyme/inhibitor label

complex, wherein the enzyme produces an electrochemical signal upon binding to a target (paragraphs 0049-0050).

Regarding claim 2, Miller et al teach the system of claim 1, wherein the probe is conjugated to the catalytic component by way of a coupling component; namely, a linker connects the enzyme to the probe (Figure 6 and paragraph 0034).

Regarding claim 3, Miller et al teach the system of claim 2, wherein the catalytic activity of the molecular switch is changed when an analyte contacts the probe; namely, upon binding of the probe to the target, the inhibitor is removed form the enzyme, thus restoring enzyme activity (paragraph 0047).

Regarding claim 4, Miller et al teach the system of claim 3, wherein the change in the catalytic activity of the molecular switch is due to a conformational change in the probe which is elicited by the analyte; namely, upon binding of the probe to the target, the conformation of the probe is altered so that the inhibitor is removed form the enzyme, thus restoring enzyme activity (paragraph 0047 and Figure 6).

Regarding claims 5-7, Miller et al teach the system of claim 1, wherein the probe is a nucleic acid; namely, a DNA molecule (i.e., claim 5; Figure 6), which is a deoxyribonucleic acid (i.e., claim 6), which is present in hybridized form because it forms a stem potion via hybridization (i.e., claim 7; Figure 6).

Regarding claims 8-9, Miller et al teach the system of claim 1, wherein the probe is an oligonucleotide; namely, a DNA molecule (Figure 6), which is a oligonucleotide (i.e., claim 8; paragraph 0028), which is exhibits an intramolecular hybridization in the form of a hybridized stem portion (i.e., claim 9; Figure 6).

Regarding claims 10 and 12, Miller et al teach the system of claim 1, wherein the catalytic component is an enzyme (Figure 6).

Regarding claim 17, Miller et al teach a molecular switch comprising a probe and a catalytic component; namely, Miller et al teach Figure 6, which comprises a probe in the form of a DNA portion and a catalytic component in the form of an enzyme/inhibitor label complex, wherein the enzyme produces an electrochemical signal upon binding to a target (paragraphs 0049-0050).

11. Claims 1-11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Lizardi (U.S. Patent No. 5,118,801, issued 2 June 1992).

Regarding claim 1, Lizardi teaches an analytical test system comprising a switch probe in the form of the probe of Figures 12-13, which comprises a probe in the form of a probe sequence 31 and a catalytic component in the form of an pre-ribozyme sequence 32 (Example V), wherein the binding of a target to the probe results in a conformational switch that activates ribozyme 36 (Figure 13 and Example V). A ribozyme is a catalytically active nucleic acid (column 13, lines 5-20).

Regarding claim 2, Lizardi teaches the system of claim 1, wherein the probe is conjugated to the catalytic component by way of a coupling component; namely, spacer sequence connects the catalytic ribozyme portion to the probe (Figure 13 and Example V).

Regarding claim 3, Lizardi teaches the system of claim 2, wherein the catalytic activity of the molecular switch is changed when an analyte contacts the probe; namely,

upon binding of the probe to the target, switch sequence 32 shifts to form ribozyme 36 (Figure 13 and Example V).

Regarding claim 4, Lizardi teaches the system of claim 3, wherein the change in the catalytic activity of the molecular switch is due to a conformational change in the probe which is elicited by the analyte; namely, upon binding of the probe to the target, the conformation of the probe switches so that switch sequence 32 shifts to form ribozyme 36 (Figure 13 and Example V).

Regarding claims 5-7, Lizardi teaches the system of claim 1, wherein the probe is a nucleic acid; namely, an RNA molecule (i.e., claim 5; Example V), which is a ribonucleic acid (i.e., claim 6), which is present in hybridized form because it forms a stem potion via hybridization (i.e., claim 7; Figure 12 and Example V).

Regarding claims 8-9, Lizardi teaches the system of claim 1, wherein the probe is an oligonucleotide; namely, a RNA molecule (Example V), which is a oligonucleotide (i.e., instant claim 8; claim 1 of Lizardi), which is exhibits an intramolecular hybridization in the form of a hybridized stem portion (i.e., claim 9; Figure 12).

Regarding claims 10 and 11, Lizardi teaches the system of claim 1, wherein the catalytic component is a catalytic nucleic acid in the form of a ribozyme (Figure 12), which is a ribonucleic acid because it is made of RNA (i.e., claim 11; Example V).

Regarding claim 17, Lizardi teaches a molecular switch comprising a probe and a catalytic component; namely, Lizardi teaches Figures 12-13, which show a probe in the form of a probe sequence 31 and a catalytic component in the form of an pre-ribozyme sequence 32 (Example V), wherein the binding of a target to the probe results in a

conformational switch that activates ribozyme 36 (Figure 13 and Example V). A ribozyme is a catalytically active nucleic acid (column 13, lines 5-20).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al (U.S. Patent Application Publication No. US 2004/0018492 A1, published 29 January 2004) in view of Lizardi (U.S. Patent No. 5,118,801, issued 2 June 1992).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiments of dependent claims 10-11.

It is also noted that while claim 10 has been rejected as anticipated by Mille et al under 35 U.S.C 102(b) as described above in Section 10, the claims is also obvious of Miller et al in view of Lizardi et al using the alternative interpretation outlined below.

Regarding claims 10-11, Miller et al teach an analytical test system comprising a switch probe in the form of the probe of Figure 6, which comprises a probe in the form of a DNA portion and a catalytic component in the form of an enzyme/inhibitor label

complex, wherein the enzyme produces an electrochemical signal upon binding to a target (paragraphs 0049-0050).

Miller et al do not teach the catalytic component is a catalytically active nucleic acid (i.e., claims 10-11).

However, Lizardi teaches a molecular switch comprising a probe and a catalytic component; namely, Lizardi teaches Figures 12-13, which show a probe in the form of a probe sequence 31 and a catalytic component in the form of an pre-ribozyme sequence 32 (Example V), wherein the binding of a target to the probe results in a conformational switch that activates ribozyme 36 (Figure 13 and Example V). A ribozyme is a catalytically active nucleic acid (column 13, lines 5-20). Lizardi also teaches the ribozyme has the added advantage of releasing an exponentially replicatable signal component (Example V), which has the benefit of increasing the sensitivity of detection (column 8, lines 40-50). Thus, Lizardi teaches the known technique of using a catalytically active nucleic acid.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the system as taught by Miller et al so that the catalytic component is the catalytically active nucleic acid as taught by Lizardi to arrive at the instantly claimed system with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a system having the added advantage of increasing the sensitivity of detection as a result of releasing an exponentially replicatable signal component as explicitly taught by Lizardi (Example V and column 8,

lines 40-50). In addition, it would have been obvious to the ordinary artisan that the known technique of using a catalytically active nucleic acid as a catalytic component on the probe as taught by Lizardi could have been applied to the system of Miller et al with predictable results because the known technique of using a catalytically active nucleic acid as a catalytic component on the probe as taught by Lizardi predictably results in the use of a reliably detectable catalytic component.

14. Claims 1, 10, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lizardi (U.S. Patent No. 5,118,801, issued 2 June 1992) in view of Miller et al (U.S. Patent Application Publication No. US 2004/0018492 A1, published 29 January 2004).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiments of dependent claims 10 and 12.

It is also noted that while claim 10 has been rejected as anticipated by Lizardi under 35 U.S.C 102(b) as described above in Section 11, the claims is also obvious of Lizardi et al in view of Miller et al using the alternative interpretation outlined below.

Regarding claims 10 and 12, Lizardi teaches an analytical test system comprising a switch probe in the form of the probe of Figures 12-13, which comprises a probe in the form of a probe sequence 31 and a catalytic component in the form of an pre-ribozyme sequence 32 (Example V), wherein the binding of a target to the probe results in a conformational switch that activates ribozyme 36 (Figure 13 and Example V). A ribozyme is a catalytically active nucleic acid (column 13, lines 5-20).

Lizardi does not teach the catalytically active component is an enzyme (i.e., claims 10 and 12).

However, Miller et al teach system comprising a switch probe in the form of the probe of Figure 6, which comprises a probe in the form of a DNA portion and a catalytic component in the form of an enzyme/inhibitor label complex, wherein the enzyme produces an electrochemical signal upon binding to a target, and which has the added advantage of providing little signal in the absence of a target (i.e., when unbound; paragraphs 0049-0050), thereby reducing the likelihood of a false positive result. Thus, Miller et al teach the known technique of using an enzyme as a catalytic component.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the system as taught by Lizardi so that the catalytic component is an enzyme as taught by Miller et al to arrive at the instantly claimed system with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a system having the added advantage of reducing the likelihood of a false positive result as a result of providing little signal when unbound as explicitly taught by Miller et al (paragraphs 0049-0050). In addition, it would have been obvious to the ordinary artisan that the known technique of using an enzyme as a catalytic component on the probe as taught by Miller et al could have been applied to the system of Lizardi with predictable results because the known technique of using an enzyme as a catalytic component on the probe as taught by Miller et al predictably results in the use of a reliably detectable catalytic component.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571)272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert T. Crow/
Examiner, Art Unit 1634

Robert T. Crow
Examiner
Art Unit 1634